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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
RAO, SAVITHA M	

ART UNIT	PAPER NUMBER
1629	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/585,609	SCHELLER, DIETER	
	Examiner	Art Unit	
	SAVITHA RAO	1629	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12/14/2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3,4 and 14-24* is/are pending in the application.

4a) Of the above claim(s) *19 and 20* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 3-4, 14-18 and 21-24* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *12/14/2009 and 03/07/2011*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 1, 3-4, and 14-24 are pending.

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 12/16/2008 has been entered.

Receipt and consideration of Applicants' amended claim set and remarks/arguments filed on filed on 12/14/2009 is acknowledged. Claims 19-20 remain withdrawn as being drawn towards a nonelected invention or specie. Claims under consideration are claims 1, 3-4, 14-18 and new claims 21-24.

Applicants' arguments, filed 12/14/2009, have been fully considered but they are not deemed to be persuasive. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

Information Disclosure Statement

The information disclosure statement (IDS) dated 12/14/2009 and 03/07/2011 complies with the provisions of 37 CFR 1.97, 1.98 and MPEP § 609. Accordingly, it has been placed in the application file and the information therein has been considered as to the merits.

Priority information

This application is a national stage entry of PCT/EP04/14656 dated 12/23/2004 which claims benefit under Title 35 U.S.C 119 to German patent application no. 103 61 258.0 filed on 12/24/2003. Certified copy of the priority document was received and has been acknowledged.

Inventorship

In view of the papers filed 07/01/2010, this non-provisional application, as filed, through error but without deceptive intent, improperly set forth the inventorship. Accordingly, this application has been corrected in compliance with 37 CFR 1.48(c). The inventorship of this application has been changed by the addition of Frank Dressen as inventor in addition to the previously listed inventor Dieter Scheller.

The application will be forwarded to the Office of Initial Patent Examination (OIPE) for issuance of a corrected filing receipt and correction of Office records to reflect the inventorship as corrected.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

(Enablement)

Claims 1, 3-4, 14-18 and new claims 21-24 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the "**treatment** of dopaminergic cell loss in a subject or decreasing the progression of Parkinson's disease", does not reasonably provide enablement for the "**Preventive treatment of Parkinson's disease**". The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

Enablement is considered in view of the Wands factors (MPEP 2164.01(a)). These include: nature of the invention, breadth of the claims, guidance of the specification, the existence of working examples, and predictability of the prior art, state of the prior art and the amount of experimentation necessary. All of the **Wands factors** have been considered with regard to the instant claims, with the most relevant factors discussed below.

Nature of the Invention: All of the rejected claims are drawn to a method for **preventive** treatment of Parkinson's disease in a subject suffering from, comprising administration of **rotigotine**. The nature of the invention is extremely complex in that it

encompasses the actual **prophylaxis** of a neurological disorder (i.e. dopaminergic cell loss) such that the subject treated with above compounds does not contract Parkinson's disease. In other words, the instant claims are drawn to a composition and method of preventing all preclinical stages of any and all stages of Parkinson's disease, which includes any undetectable stages of the disease.

Breath of the Claims*:* The complex of nature of the claims greatly exacerbated by breath of the claims. The claims encompass prevention of a complex cell degenerative disorder in humans which has potentially many different causes (i.e. many different mutations or combination of mutations). Each of which may or may not be addressed by the administration of the claimed compounds.

Guidance of the Specification and working examples: The guidance given by the specification as to how one would administer the claimed compounds to a subject in order to actually prevent Parkinson's is minimal. All of the guidance provided by the specification is directed towards **treatment rather than prophylaxis** of dopaminergic cell loss (i.e. Parkinson's disease). The examples recited in the instant disclosure recites treatment of animals in which experimental Parkinsonism's were generated by treating them with MPTP neurotoxin. The data presented just demonstrates the neuroprotective nature of rotigotine. It is noted that in instant disclosure does not present any examples or data showing the effect of the instantly claimed compound in preventing Parkinson's disease where in patients without clinically confirmed Parkinson's disease are treated with the instantly claimed drug.

The state of the prior art and the predictability or lack thereof in the art:

The state of the prior art is such that it involves screening both *in vitro* and *in vivo* to determine which compounds exhibit the desired pharmacological activities (i.e. which compounds treat which specific disease). There is no absolute predictability even in view of the seemingly high level of skill in the art. The existence of these obstacles establishes that the contemporary knowledge in the art would prevent one of ordinary skill in the art from accepting any therapeutic or preventive regimen on its face.

While the state of the art is relatively high with regard to **treatment** of neurodegenerative disorders (i.e. Parkinson's disease), the state of the art with regard to **prevention** of such disorders is underdeveloped. In particular, there do not appear to be any examples or teachings in the prior art wherein a compound similar to the claimed compounds was administered to a subject to **prevent** development of Parkinson's disease. The state of the art, Kase et al. (US 2004/0198753A1) teach that there is **no known cure** for Parkinson's disease and the treatment is **aimed at controlling the symptoms**. Kase et al. teach that most early Parkinson's disease patients respond well to symptomatic treatment with dopamine replacement therapy, but **disability increases with progression of the disease**. (Page 1, [0010]).

The lack of significant guidance from the specification or prior art with regard to the actual **prevention** of Parkinson's disease in a human subject with the claimed compounds makes practicing the claimed invention unpredictable in terms of **prevention of Parkinson's disease**.

The amount of Experimentation Necessary: In order to practice claimed invention, one of skilled in the art would have to first envision a combination of appropriate pharmaceutical carrier, compound dosage, duration of treatment, route of administration, etc. and appropriate animal model system for one of the claimed compounds and test the combination in the model system to determine whether or not the combination is effective for prevention of Parkinson's disease. If unsuccessful, which is likely given the lack of significant guidance from the specification or prior art regard prevention of Parkinson's disease with any compound, one of skill in the art would have to then either envision a modification of the first combination of pharmaceutical compound, compound dosage, duration of treatment, route of administration, etc. and appropriate animal model system, or envision an entirely new combination of the above, and test the system again. If again unsuccessful, which is likely given the lack of significant guidance form the specification of prior art regarding prevention of Parkinson's disease with any compound, the entire, unpredictable process would have to be repeated until successful. Therefore, it would require undue, unpredictable experimentation to practice the claimed invention to prevent the development of Parkinson's disease in a subject by administration of the claimed compound.

Thus, factors such as "sufficient working examples", "the level of skill in the art", and "predictability", etc. have been demonstrated to be sufficiently lacking in the instant claimed methods. In view of the breadth of the claims, the chemical nature of the invention, and the lack of working examples regarding the activity of the claimed

compound or combination of compounds, one having ordinary skill in the art would have to undergo an undue amount of experimentation to use the invention commensurate with the scope of the claims.

Genetech Inc. V. Novo Nordisk A/S (CA FC) 42 USPQ2d 1001, states that "a patent is not a hunting license. It is not a reward for search, but compensation for its successful conclusion" and "[p]atent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable".

Therefore, in view of the Wands factors discussed above, to practice the claimed invention herein, a person of skill in the art would have to engage in undue experimentation to test which diseases can be treated or prevented by the compound encompasses in the instant claims, with no assurance of success. Thus, rejection of claims 12-13 under 35 U.S.C. §112, first paragraph, is deemed proper

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims , 1, 3-4, 14-18 and new claims 21-24 are rejected under 35 U.S.C. 103(a) as being unpatentable over Li et al. (U.S.Patent No. 7,632,852, referenced in the instant IDS) in view of Gerlach et al. (2003, referenced in instant IDS) of and Guttman (2003, already of record).

Li et al. teach that Parkinson's disease is caused by **the degeneration of dopaminergic neurons** (column 1, lines 12-15). Li et al. teach that the Parkinson's disease is characterized by major clinical features including tremor, bradykinesia, rigidity, dyskinesia, gait disturbances, and speech disorders. In some patients, dementia may accompany these symptoms. Involvement of the autonomic nerve system may produce orthostatic hypotension, paroxysmal flushing, problems with thermal regulation, constipation, and loss of bladder and sphincter control. Psychological disorders such as loss of motivation and depression may also accompany Parkinson's disease (column 1, lines 23-32). Li et al. teach that Parkinson's disease is primarily a disease of middle age and beyond, and it affects both men and women equally. The highest rate of occurrence of Parkinson's disease is in the age group over 70 years old. The mean age at onset is between 58 and 62 years of age,

and most patients develop Parkinson's disease between the age of 50 and 79. Early motor deficits of Parkinson's disease can be traced to incipient degeneration of nigra dopamine-releasing cells. This neuronal degeneration produces a defect in the dopaminergic pathway that connects the substantial nigra to the stratum. As the disease progresses, refractory motor, autonomic, and mental abnormalities may develop, which implies that there is progressive degeneration of striatal receptor mechanisms. Li et al. teach that rotigotine is a dopamine agonist that is effective for the treatment of the symptoms of Parkinson's disease (column 2, lines 21-39). Li et al. teach that Parkinson's disease is known to be gradual in onset and progressive and variable in clinical manifestation. Evidence suggests that striatal dopamine content declines to 20% below levels found in age-matched controls before symptoms occur (column 1, lines 49-54). Li et al. teach that Parkinson's disease, there are the broad ranges of symptoms and differing severity (column 3, lines 32-34).

Li et al. do not teach that expressly teach the administration of rotigotine to the subject who does not have clinically evident Parkinson's disease, the administration of rotigotine to the subject who has at least one clinical symptom selected from the group consisting of an olfactory disorder, depression, a sleep disorder of the "REM behavior disorder" type, constipation and a short-term movement anomaly (Instant claim 3) ; Does not teach the subject without any of four cardinal symptoms of Parkinson's disease set forth in instant claim 22; and the subject exhibits a mutation of the gene and/or alteration of neuromelanin pattern set forth in claims 4 and 23.

Gerlach et al. teach that biochemical markers, such as **neuromelanin** can be used or diagnostic markers in Parkinson's disease. (abstract, title).

Guttman et al. teach that genetic markers such as the **PARK genes 1-8** can be used in the diagnosis and management of Parkinson's disease (title, abstract).

It would have been obvious to one of ordinary skill in the art to administer rotigotine to the subject who does not have clinically confirmed Parkinson's disease to provide neuroprotection against dopaminergic neuron loss because rotigotine is effective for the treatment of Parkinson's disease which is characterized by degeneration of dopaminergic neuron and because the subjects with Parkinson's disease can be detected before the clinical symptoms occur by measurement of striatal dopamine content as taught by Li et al. One would have been motivated to employ rotigotine for the treatment of dopaminergic neuron loss in the subjects before they actually exhibit the clinically evident symptoms of Parkinson's disease. With regard to the subject without any of the four cardinal symptoms of Parkinson's disease set forth in instant claim 22, such is obvious because there is a broad range of symptoms of Parkinson;s disease and differing in severity and Li et al. teaches , One would have been motivated to treat those patients having various severities including partial degree of severity in those symptoms described by Li et al. in order to achieve an expected benefit of rotigotine in the treatment of dopaminergic neuron degeneration. With regard to the subject exhibits the mutation and alterations set forth in claim 4 and 23, such is obvious because the mutations and alteration set forth in these claims is the marker and indications of presence of Parkinson's disease as taught by Gerlach et al. and Guttman.

One would have been motivated to employ those subjects exhibiting the mutations and alterations set forth in instant claims in order to achieve an expected beneficial effect of rotigotine in the treatment of dopaminergic neuron degeneration in Parkinson's disease patients taught by Li et al.

Conclusion

Claims 1, 3-4, 14-18 and new claims 21-24.are rejected. No claims are allowed

Any inquiry concerning this communication or earlier communications from the examiner should be directed to SAVITHA RAO whose telephone number is (571)270-5315. The examiner can normally be reached on Mon-Fri 7 am to 4 pm. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Lundgren can be reached at 571-272-5541. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/SAVITHA RAO/
Examiner, Art Unit 1629